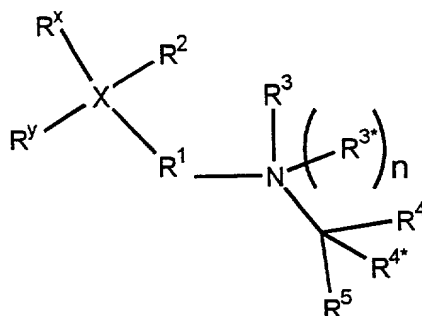


What is claimed:

1. A compound of the following formula:



or a pharmaceutically acceptable salt thereof,

- 5 wherein:

- (1) X is nitrogen or carbon, and  $R^2$  is not present when X is nitrogen;
- (2)  $R^2$  (a) is hydrogen, (C1-C6) alkyl, (C1-C6) alkoxy, cyano, (C2-C7) alkanoyl, aminocarbonyl, (C1-C6) alkylaminocarbonyl or dialkylaminocarbonyl wherein each alkyl is independently C1 to C6, (b) comprises (where  $R^1$  is not aminoethylene,  $-O-R^8$  or  $-S-R^{8*}$ )
- 10 hydroxy, fluoro, chloro, bromo or (C2-C7) alkanoyloxy, (c) forms a double bond with an adjacent carbon or nitrogen from one of either  $R^1$ ,  $R^{xb}$  or  $R^{yb}$ , or (d) is  $R^{2a}$  linked by  $R^{2b}$  to X;
- (2i)  $R^x$  is  $R^{xa}$  linked by  $R^{xb}$  to X;
- (2ii)  $R^y$  is  $R^{ya}$  linked by  $R^{yb}$  to X;
- (2iii)  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$ , are independently aryl, heteroaryl, adamantyl or a 5 to 7-membered
- 15 non-aromatic ring having from 0 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, wherein:
- (a) aryl is phenyl or naphthyl,
- (b) heteroaryl comprises a five-membered ring, a six-membered ring, a six-membered ring fused to a five-membered ring, a five-membered ring fused to a six-membered ring, or a six-membered ring fused to a six-membered ring, wherein the heteroaryl
- 20 is aromatic and contains heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, with the remaining ring atoms being carbon,
- (c) each of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  can be independently substituted with one of  $R^q$ ,  $R^rO-$  or  $R^sS-$ , wherein each of  $R^q$ ,  $R^r$  and  $R^s$  are independently aryl, heteroaryl,
- 25 adamantyl or a 5 to 7-membered non-aromatic ring as these ring structures are defined for  $R^{xa}$ , and

(d)  $R^{xa}$ ,  $R^{ya}$ ,  $R^{2a}$ ,  $R^q$ ,  $R^r$  and  $R^s$  can be additionally substituted with one or more substituents selected from the group consisting of fluoro, chloro, bromo, nitro, hydroxy, cyano, trifluoromethyl, amidosulfonyl which can have up to two independent (C1-C6) N-alkyl substitutions, adamantyl, (C1-C12) alkyl, (C1-C12) alkenyl, amino, (C1-C6) alkylamino, dialkylamino wherein each alkyl is independently C1 to C6, (C1-C6) alkoxy, (C2-C7) alkanoyl, (C2-C7) alkanoyloxy, trifluoromethoxy, hydroxycarbonyl, (C2-C7) alkylloxycarbonyl, aminocarbonyl that can be substituted for hydrogen with up to two independent (C1-C6) alkyl, (C1-C6) alkylsulfonyl, amidino that can independently substituted with up to three (C1-C6) alkyl, or methylenedioxy or ethylenedioxy with the two oxygens bonded to adjacent positions on the aryl or heteroaryl ring structure, which methylenedioxy or ethylenedioxy can be substituted with up to two independent (C1-C6) alkyl, wherein:

(i.) the substitutions of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  can be combined to form a second bridge between two of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  comprising (1) (C1-C2) alkyl or alkenyl, which can be independently substituted with one or more (C1-C6) alkyl, (2) sulfur, (3) oxygen, (4) amino, which can be substituted for hydrogen with one (C1-C6) alkyl, (5) carbonyl, (6)  $-CH_2C(=O)-$ , which can be substituted for hydrogen with up to two independent (C1-C6) alkyl, (7)  $-C(=O)-O-$ , (8)  $-CH_2-O-$ , which can be substituted for hydrogen with up to two independent (C1-C6) alkyl, (9)  $-C(=O)N(R^{24})$ , wherein  $R^{24}$  is hydrogen or (C1-C6) alkyl, (10)  $-CH_2-NH-$ , which can be substituted for hydrogen with up to three (C1-C6) alkyl, or (11)  $-CH=N-$ , which can be substituted for hydrogen with (C1-C6) alkyl, or wherein two of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  can be directly linked by a single bond;

(2iv)  $R^{xb}$  and  $R^{2b}$  are independently a single bond or (C1-C2) alkylene:

(2v)  $R^{yb}$  is a single bond, oxa, (C1-C2) alkylene, ethenylene or  $-CH=$  (where the double bond is with X), thia, methyleneoxy or methylenethio, or either  $-N(R^6)$  or  $-CH_2-N(R^{6*})-$ , wherein  $R^6$  and  $R^{6*}$  are hydrogen or (C1-C6) alkyl, wherein when X is nitrogen X is not bonded to another heteroatom;

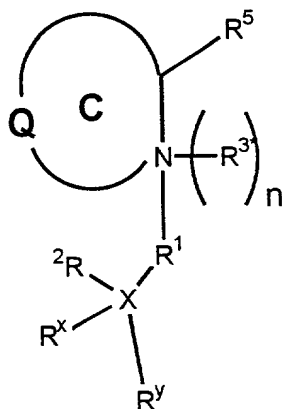
- (3)  $R^1$  comprises: a straight-chained (C2-C3) aliphatic group; where X is carbon, =N-O-(ethylene), wherein the unmatched double bond is linked to X; (where X is carbon and  $R^{yb}$  does not include a heteroatom attached to X), -O- $R^8$  or -S- $R^{8*}$  wherein  $R^8$  or  $R^{8*}$  is a ethylene or ethenylene and O or S is bonded to X; (where X is carbon and  $R^{yb}$  does not include a heteroatom attached to X), aminoethylene where the amino is bonded to X:

wherein  $R^1$  can be substituted with up to one hydroxy, up to one (C1-C6) alkoxy or up to one (C2-C7) alkanoyloxy, with up to two independent (C1-C6) alkyl, with up to one oxo, up to one (C1-C6) alkylidene, with the proviso that the hydroxy, alkoxy, alkanoyloxy or oxo substituents are not bonded to a carbon that is bonded to a nitrogen or oxygen;

wherein the alkyl or alkylidene substituents of  $R^1$  can be linked to form a 3 to 7-membered non-aromatic ring; and

wherein if X is nitrogen, X is linked to  $R^1$  by a single bond and the terminal carbon of  $R^1$  that links  $R^1$  to N is saturated;

- (4)  $R^3$  (a) is hydrogen, (C1-C6) alkyl, or phenyl or phenylalkyl wherein the alkyl is C1 to C6 and either such phenyl can be substituted with the same substituents defined above for the aryl or heteroaryl of  $R^{xa}$ , (b) is  $-R^{12}Z(R^{xx})(R^{yy})(R^{11})$ , wherein  $R^{12}$  is bonded to N, Z is independently the same as X,  $R^{xx}$  is independently the same as  $R^x$ ,  $R^{yy}$  is independently the same as  $R^y$ ,  $R^{11}$  is independently the same as  $R^2$  and  $R^{12}$  is independently the same as  $R^1$ , or (c) forms, together with  $R^4$ , a ring C, as follows:



, wherein  $R^{4*}$  is hydrogen when ring C is present;

- (5) n is 0 or 1, and where if n is 1,  $R^{3*}$  is either (C1-C6) alkyl (with the attached nitrogen having a positive charge) or oxygen (forming an N-oxide) and X is carbon;

(5') Q together with the illustrated ring nitrogen and ring carbon bearing  $R^5$  form ring C, wherein ring C is a 3 to 8-membered ring, a 3 to 8-membered ring substituted with a 3 to 6-membered spiro ring, or a 3 to 8-membered ring fused with a 5 to 6-membered ring, wherein the fused ring lacking the illustrated ring nitrogen can be aromatic or heteroaromatic, wherein for each component ring of ring C there are up to two heteroatoms selected from oxygen, sulfur or nitrogen, including the illustrated nitrogen, and the rest carbon, with the proviso that the ring atoms include no quaternary nitrogens other than the illustrated nitrogen, with the proviso that, in saturated rings, ring nitrogen atoms are separated from other ring heteroatoms by at least two intervening carbon atoms:

10 wherein the carbon and nitrogen ring atoms of ring C can be substituted with substituents selected from (C1-C6) alkyl, (C2-C6) alkenylene, cyano, nitro, trifluoromethyl, (C2-C7) alkylloxycarbonyl, (C1-C6) alkylidene, hydroxyl, (C1 - C6) alkoxy, oxo, hydroxycarbonyl, aryl wherein the aryl is as defined for  $R^{xa}$  or heteroaryl wherein the heteroaryl is as defined for  $R^{xa}$ , with the proviso that ring atoms substituted with alkylidene, hydroxycarbonyl or oxo are carbon, with the further proviso that ring atoms substituted with hydroxyl or alkoxy are separated from other ring heteroatoms by at least two intervening carbon atoms;

(6)  $R^4$  and  $R^{4*}$  are independently hydrogen or (C1-C6) alkyl, or one of  $R^4$  and  $R^{4*}$  can be (C1-C6) hydroxyalkyl; and

20 (7)  $R^5$  is (CO)NR<sup>13</sup>R<sup>14</sup>, (CO)OR<sup>15</sup>, (CO)SR<sup>16</sup>, (SO<sub>2</sub>)NR<sup>17</sup>R<sup>18</sup>, (PO)(OR<sup>19</sup>)(OR<sup>20</sup>), (CR<sup>22</sup>)(OR<sup>23</sup>)(OR<sup>24</sup>), CN or tetrazol-5-yl, wherein  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$  and  $R^{20}$  are independently hydrogen, (C1-C8) alkyl which can include a (C3-C8) cycloalkyl, wherein the carbon linked to the oxygen of  $R^{15}$  or the sulfur of  $R^{16}$  has no more than secondary branching and, (C2-C6) hydroxyalkyl, aminoalkyl where the alkyl is C2 to C6 and the amino can be substituted with up to two independent (C1-C6) alkyls, arylalkyl wherein the alkyl is C1-C6, heteroarylalkyl wherein the alkyl is C1 to C6, aryl or heteroaryl,  $R^{22}$  is hydrogen or OR<sup>25</sup> and  $R^{23}$ ,  $R^{24}$  and  $R^{25}$  are (C1-C6) alkyl, phenyl, benzyl, acetyl or, where  $R^{22}$  is hydrogen, the alkyls of  $R^{23}$  and  $R^{24}$  can be combined to include 1,3-dioxolane or 1,3-dioxane:

30 wherein the aryl is phenyl or naphthyl and the heteroaryl is a five-membered ring, a six-membered ring, a six-membered ring fused to a five-membered ring, a five-membered ring fused to a six-membered ring, or a six-membered ring fused to a six-membered ring, wherein the heteroaryl is aromatic and contains heteroatoms

selected from the group consisting of oxygen, sulfur and nitrogen, with the remaining ring atoms being carbon;

wherein the aryl, heteroaryl, aryl of arylalkyl or the heteroaryl of heteroarylalkyl can be substituted with substituents selected from the group consisting of fluoro, chloro, bromo, nitro, cyano, hydroxy, trifluoromethyl, amidosulfonyl which can have up to two independent (C1-C6) N-alkyl substitutions, (C1-C6) alkyl, (C2-C6) alkenyl, (C1-C6) alkylamine, dialkylamine wherein each alkyl is independently C1 to C6, amino, (C1-C6) alkoxy, (C2-C7) alkanoyl, (C2-C7) alkanoyloxy, trifluoromethoxy, hydroxycarbonyl, (C2-C7) alkyloxycarbonyl, aminocarbonyl that can be N-substituted with up to two independent (C1-C6) alkyl, (C1-C6) alkylsulfonyl, amidino that can substituted with up to three (C1-C6) alkyl, or methylenedioxy or ethylenedioxy with the two oxygens bonded to adjacent positions on the aryl or heteroaryl ring structure, which methylenedioxy or ethylenedioxy can be substituted with up to two independent (C1-C6) alkyl;

wherein  $R^{13}$  and  $R^{14}$  together with the nitrogen can form a 5 to 7-membered ring that can contain one additional heteroatom selected from oxygen and sulfur;

wherein if  $R^{15}$  is hydrogen and  $R^1$  is propylene, then at least one of the following applies

- (1) both  $R^X$  and  $R^Y$  are not *p*-fluorophenyl, (2) one of  $R^X$  and  $R^Y$  includes a heteroaryl, (3)  $R^Y$  is arylalkyl, heteroarylalkyl, aryloxy, heteroaryloxy, arylmethoxy, heteroarylmethoxy, arylthio, heteroarylthio, arylmethylthio, heteroaryl methylthio,  $Ar-N(R^6)-$  or  $Ar-CH_2-N(R^{6*})-$ , (4)  $R^2$  is  $R^{xa} R^{xb}-$ , (5)  $R^{2*}$  is not hydrogen, (6)  $R^3$  is not hydrogen, (7) *n* is one, or (8)  $R^3$  and  $R^4$  form ring Q;

wherein if  $R^{15}$  is hydrogen and  $R^1$  is ethylene or  $X-R^1$  is prop-1-enylene, then at least

- one of the following applies (1) an aryl of at least one of  $R^X$  and  $R^Y$  is substituted with a radical different from hydrogen, (2) one of  $R^X$  and  $R^Y$  comprises a heteroaryl, (3)  $R^Y$  is arylalkyl, heteroarylalkyl, aryloxy, heteroaryloxy, arylmethoxy, heteroarylmethoxy, arylthio, heteroarylthio, arylmethylthio, heteroaryl methylthio,  $Ar-N(R^6)-$  or  $Ar-CH_2-N(R^{6*})-$ , (4)  $R^2$  is  $R^{xa} R^{xb}-$ , (5)  $R^{2*}$  is not hydrogen, (6)  $R^3$  is not hydrogen, (7) *n* is one, or (8)  $R^3$  and  $R^4$  form ring Q;

wherein if  $R^5$  is  $C(O)NH_2$ , then at least one of the following applies (1) an aryl of at least one of  $R^X$  and  $R^Y$  is substituted with a radical different from hydrogen, (2) one of  $R^X$  and  $R^Y$  comprises a heteroaryl, (3)  $R^Y$  is arylalkyl, heteroarylalkyl, aryloxy, heteroaryloxy, arylmethoxy, heteroarylmethoxy, arylthio, heteroarylthio, arylmethylthio, heteroaryl-methylthio,  $Ar-N(R^6)-$  or  $Ar-CH_2-N(R^{6*})-$ , (4)  $R^2$  is  $R^{xa} R^{xb}-$ , (5)  $R^{2*}$  is not hydrogen, (6)  $R^3$  is not hydrogen, (7)  $n$  is one, (8)  $R^1$  is not ethylene, or (9)  $R^3$  and  $R^4$  form ring Q;

wherein if  $R^{13}$  is hydrogen and  $R^{14}$  is (3,4-dihydro-2H-1-benzopyran-4-yl)methylene, then at least one of the following applies (1) an aryl of at least one of  $R^X$  and  $R^Y$  is substituted with a radical different from hydrogen, (2) one of  $R^X$  and  $R^Y$  comprises a heteroaryl, (3)  $R^Y$  is arylalkyl, heteroarylalkyl, aryloxy, heteroaryloxy, arylmethoxy, heteroarylmethoxy, arylthio, heteroarylthio, arylmethylthio, heteroaryl-methylthio,  $Ar-N(R^6)-$  or  $Ar-CH_2-N(R^{6*})-$ , (4)  $R^2$  is  $R^{xa} R^{xb}-$ , (5)  $R^{2*}$  is not hydrogen, (6)  $R^3$  is not ethyl, (7)  $n$  is one, or (8)  $R^3$  and  $R^4$  form ring Q; and

wherein if  $R^2$  is phenyl, *p*-methylphenyl or *p*-methoxyphenyl, then at least one of the following applies (1) the aryls of  $R^X$  and  $R^Y$  are not substituted with *p*-methylphenyl or *p*-methoxyphenyl, (2) an aryl of at least one of  $R^X$  and  $R^Y$  is substituted with a radical different from hydrogen, (3) one of  $R^X$  and  $R^Y$  comprises a heteroaryl, (4)  $R^Y$  is arylalkyl, heteroarylalkyl, aryloxy, heteroaryloxy, arylmethoxy, heteroarylmethoxy, arylthio, heteroarylthio, arylmethylthio, heteroaryl-methylthio,  $Ar-N(R^6)-$  or  $Ar-CH_2-N(R^{6*})-$ , (5)  $R^1$  is not aminoethylene,  $OR^8$  or  $SR^{8*}$ , (6)  $n$  is one, or (7)  $R^3$  and  $R^4$  form ring Q.

2. The compound of claim 1, the ring Q is a 4 to 8-membered ring that includes the illustrated ring nitrogen, with the remaining ring atoms being carbon.

3. The compound of claim 1, wherein (A) at least one of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  is substituted with fluoro, chloro, bromo, hydroxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, (C3-C8) alkyl,  $R^9$ ,  $R^{10}-$ ,  $R^{11}S-$ , (B)  $R^3$  is hydrogen, (C1-C6) alkyl, or phenyl or phenylalkyl wherein the alkyl is C1 to C6 and either such phenyl can be substituted with the same substituents defined above for the aryl or heteroaryl of  $R^{xa}$  or (C) the ring structures of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$ ,

including substituents thereto, otherwise include at least two aromatic ring structures that together include from 15 to 20 ring atoms.

4. The compound of claim 3, wherein at least one of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  is substituted with fluoro, trifluoromethyl, trifluoromethoxy, nitro, cyano, or (C3-C8) alkyl.

5           5. The compound of claim 1, wherein at least one of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  is substituted with  $R^q$ ,  $R^tO-$ , or  $R^sS-$ .

6. The compound of claim 1, wherein an aryl or heteroaryl of at least one of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  is phenyl.

7. The compound of claim 1, wherein  $R^{yb}$  is oxa, methyleneoxy, thia,  
10 methylenethia.

8. The compound of claim, wherein  $R^{yb}$  is oxa or thia.

9. The compound of claim 1, wherein  $R^5$  is  $(CO)NR^{13}R^{14}$ ,  $(CO)OR^{15}$  or  $(CO)SR^{16}$ .

10. The compound of claim 9, wherein  $R^{15}$  is (C2-C6) alkyl, (C2-C4)  
15 hydroxyalkyl, phenyl, phenylalkyl wherein the alkyl is C1-C3, or aminoalkyl where the alkyl is C2-C6 and the amino can be substituted with up to two independent (C1-C3) alkyls, wherein the phenyl or the phenyl of phenylalkyl can be substituted.

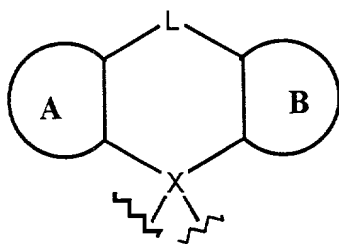
11. The compound of claim 9, wherein  $R^{15}$  is hydrogen.

12. The compound of claim 1, wherein  $R^4$  is hydrogen, methyl or hydroxymethyl  
20 and  $R^{4*}$  is hydrogen.

13. The compound of claim 1, wherein at least one of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  is a heteroaryl comprising diazolyl, triazolyl, tetrazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, thieryl, diazinyl, triazinyl, benzoazolyl, benzodiazolyl, benzothiazolyl, benzoxazolyl, benzoxolyl, benzothieryl, quinolyl, isoquinolyl, benzodiazinyl, benzotriazinyl, pyridyl, thienyl, furanyl,  
25 pyrrolyl, indolyl, isoindolyl or pyrimidyl.

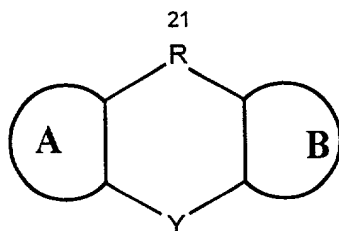
14. The compound of claim 1, wherein  $R^1$  is  $-O-R^8$  or  $-S-R^{8*}$ .

15. The compound of claim 1, wherein said second bridge between two of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  is L, and satisfies the following formula:



, wherein A and B are aryl or heteroaryl groups of  $R^{xa}$  and  $R^{ya}$ , respectively.

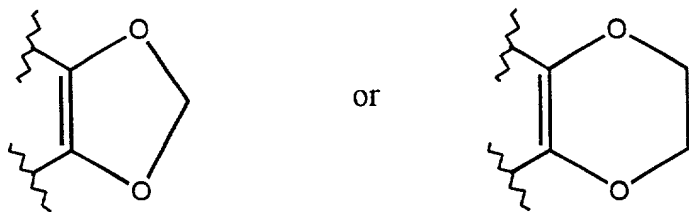
16. The compound of claim 14, wherein  $R^{xa}$ - $R^{xb}$ -,  $R^{ya}$ - $R^{yb}$ - and X form:



5 wherein Y is a carbon bonded to  $R^1$  by a single or double bond or a nitrogen that is bonded to  $R^1$  and wherein  $R^{21}$  either (i.) completes a single bond linking two aryl or heteroaryl rings of  $R^x$  and  $R^y$ , (ii.) is (C1-C2) alkylene or alkenylene, (iii.) is sulfur or (iv.) is oxygen, and wherein  $R^x$  and  $R^y$  can be substituted as set forth above.

17. The compound of claim 16, wherein  $R^{21}$  is  $CH_2CH_2$  or  $CH=CH$ .

10 18. The compound of claim 1, wherein the alkylenedioxy substitution of  $R^{xa}$ ,  $R^{ya}$  or  $R^{2a}$  is as follows:



wherein the alkylenedioxy can be substituted with up to two independent (C1-C3) alkyl.

15 19. The compound of claim 1, wherein  $R^{xa}$  and  $R^{ya}$  together can be substituted with up to six substituents,  $R^{2a}$ ,  $R^q$ ,  $R^r$  and  $R^s$  can each be substituted with up to 3 substituents, and wherein the presence of each of  $R^q$ ,  $R^r$  or  $R^s$  is considered a substitution to the respective ring structure of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$ .

20. The compound of claim 1, wherein a phenyl of  $R^3$  is substituted with up to three substituents.



21. The compound of claim 1, wherein the aryl, heteroaryl, aryl of arylalkyl or the heteroaryl of heteroarylalkyl of R<sup>13</sup>, R<sup>14</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup> or R<sup>20</sup> is substituted with up to three substituents.

22. The compound of claim 1, wherein the compound is an optically pure  
5 enantiomer.

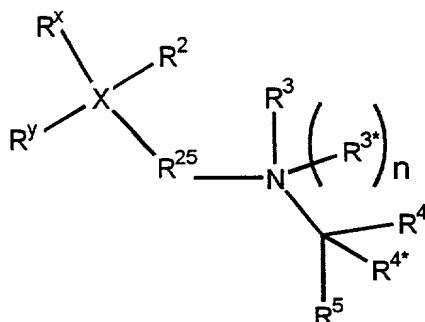
23. A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable excipient.

24. The pharmaceutical composition of claim 23, wherein the compound of claim 1 is present in an effective amount for:

- 10 (1) treating or preventing schizophrenia,
- (2) enhancing treating or preventing dementia,
- (3) treating or preventing epilepsy,
- (4) treating or preventing spasticity,
- (5) treating or preventing muscle spasm,
- 15 (6) treating or preventing pain,
- (7) preventing neural cell death after stroke,
- (8) preventing neural cell death in an animal suffering from a neurodegenerative disease,
- (9) treating or preventing mood disorders,
- 20 (10) enhancing memory or learning, or
- (11) treating or preventing learning disorders.

25 25. A method (1) of treating or preventing schizophrenia comprising administering a schizophrenia treating or preventing effective amount of a compound, (2) of treating or preventing dementia comprising administering a dementia treating or preventing effective amount of a  
30 compound, (3) of treating or preventing epilepsy comprising administering an epilepsy treating or preventing effective amount of a compound, (4) of treating or preventing spasticity comprising administering a spasticity treating or preventing effective amount of a compound, (5) of treating or preventing muscle spasm comprising administering a muscle spasm treating or preventing effective amount of a compound, (6) of treating or preventing pain comprising administering a pain treating  
or preventing effective amount of a compound, (7) of preventing neural cell death after stroke comprising administering a neural cell death preventing effective amount of a compound, (8) of preventing neural cell death in an animal suffering from a neurodegenerative disease, (9) treating or preventing mood disorders. (10) enhancing memory or learning, or (11) treating or preventing

learning disorders, comprising administering an amount effective for said treating, preventing or enhancing of a compound of formula:



or a pharmaceutically acceptable salt thereof,

- 5 (1) X is nitrogen or carbon, and  $R^2$  is not present when X is nitrogen;
- (2)  $R^2$  (a) is hydrogen, (C1-C6) alkyl, (C1-C6) alkoxy, cyano, (C2-C7) alkanoyl, aminocarbonyl, (C1-C6) alkylaminocarbonyl or dialkylaminocarbonyl wherein each alkyl is independently C1 to C6, (b) comprises (where  $R^1$  is not aminoethylene,  $-O-R^8$  or  $-S-R^{8*}$ ) hydroxy, fluoro, chloro, bromo or (C2-C7) alkanoyloxy, (c) forms a double bond with an adjacent
- 10 carbon or nitrogen from one of either  $R^1$ ,  $R^{xb}$  or  $R^{yb}$ , or (d) is  $R^{2a}$  linked by  $R^{2b}$  to X;
- (2<sup>i</sup>)  $R^x$  is  $R^{xa}$  linked by  $R^{xb}$  to X;
- (2<sup>ii</sup>)  $R^y$  is  $R^{ya}$  linked by  $R^{yb}$  to X;
- (2<sup>iii</sup>)  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$ , are independently aryl, heteroaryl, adamantyl or a 5 to 7-membered non-aromatic ring having from 0 to 2 heteroatoms selected from the group consisting of oxygen,
- 15 sulfur and nitrogen, wherein:
  - (a) aryl is phenyl or naphthyl,
  - (b) heteroaryl comprises a five-membered ring, a six-membered ring, a six-membered ring fused to a five-membered ring, a five-membered ring fused to a six-membered ring, or a six-membered ring fused to a six-membered ring, wherein the heteroaryl is aromatic and contains heteroatoms selected from the group consisting of
  - 20 oxygen, sulfur and nitrogen, with the remaining ring atoms being carbon,
  - (c) each of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  can be independently substituted with one of  $R^q$ ,  $R^fO-$  or  $R^{ss}-$ , wherein each of  $R^q$ ,  $R^f$  and  $R^s$  are independently aryl, heteroaryl, adamantyl or a 5 to 7-membered non-aromatic ring as these ring structures are
  - 25 defined for  $R^{xa}$ , and
  - (d)  $R^{xa}$ ,  $R^{ya}$ ,  $R^{2a}$ ,  $R^q$ ,  $R^f$  and  $R^s$  can be additionally substituted with one or more substituents selected from the group consisting of fluoro, chloro, bromo, nitro,

hydroxy, cyano, trifluoromethyl, amidosulfonyl which can have up to two independent (C1-C6) N-alkyl substitutions, adamantyl, (C1-C12) alkyl, (C1-C12) alkenyl, amino, (C1-C6) alkylamino, dialkylamino wherein each alkyl is independently C1 to C6, (C1-C6) alkoxy, (C2-C7) alkanoyl, (C2-C7) alkanoyloxy, trifluoromethoxy, hydroxycarbonyl, (C2-C7) alkyloxycarbonyl, aminocarbonyl that can be substituted for hydrogen with up to two independent (C1-C6) alkyl, (C1-C6) alkylsulfonyl, amidino that can independently substituted with up to three (C1-C6) alkyl, or methylenedioxy or ethylenedioxy with the two oxygens bonded to adjacent positions on the aryl or heteroaryl ring structure, which methylenedioxy or ethylenedioxy can be substituted with up to two independent (C1-C6) alkyl, wherein:

(i.) the substitutions of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  can be combined to form a second bridge between two of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  comprising (1) (C1-C2) alkyl or alkenyl, which can be independently substituted with one or more (C1-C6) alkyl, (2) sulfur, (3) oxygen, (4) amino, which can be substituted for hydrogen with one (C1-C6) alkyl, (5) carbonyl, (6)  $-CH_2C(=O)-$ , which can be substituted for hydrogen with up to two independent (C1-C6) alkyl, (7)  $-C(=O)-O-$ , (8)  $-CH_2-O-$ , which can be substituted for hydrogen with up to two independent (C1-C6) alkyl, (9)  $-C(=O)N(R^{24})$ , wherein  $R^{24}$  is hydrogen or (C1-C6) alkyl, (10)  $-CH_2-NH-$ , which can be substituted for hydrogen with up to three (C1-C6) alkyl, or (11)  $-CH=N-$ , which can be substituted for hydrogen with (C1-C6) alkyl, or wherein two of  $R^{xa}$ ,  $R^{ya}$  and  $R^{2a}$  can be directly linked by a single bond;

(2<sup>iv</sup>)  $R^{xb}$  and  $R^{2b}$  are independently a single bond or (C1-C2) alkylene;

(2<sup>v</sup>)  $R^{yb}$  is a single bond, oxa, (C1-C2) alkylene, ethenylene or  $-CH=$  (where the double bond is with X), thia, methyleneoxy or methylenethio, or either  $-N(R^6)$  or  $-CH_2-N(R^{6*})-$ , wherein  $R^6$  and  $R^{6*}$  are hydrogen or (C1-C6) alkyl, wherein when X is nitrogen X is not bonded to another heteroatom;

(3)  $R^l$  comprises: a straight-chained (C2-C3) aliphatic group; where X is carbon,  $=N-O-(ethylene)$ , wherein the unmatched double bond is linked to X; (where X is carbon and  $R^{yb}$  does not include a heteroatom attached to X),  $-O-R^8$  or  $-S-R^{8*}$  wherein  $R^8$  or  $R^{8*}$  is a ethylene or

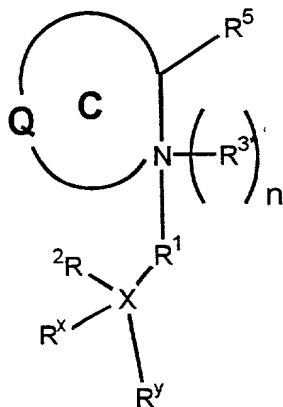
ethenylene and O or S is bonded to X; (where X is carbon and R<sup>y</sup><sup>b</sup> does not include a heteroatom attached to X), aminoethylene where the amino is bonded to X:

wherein R<sup>1</sup> can be substituted with up to one hydroxy, up to one (C1-C6) alkoxy or up to one (C2-C7) alkanoyloxy, with up to two independent (C1-C6) alkyl, with up to one oxo, up to one (C1-C6) alkylidene, with the proviso that the hydroxy, alkoxy, alkanoyloxy or oxo substituents are not bonded to a carbon that is bonded to a nitrogen or oxygen;

wherein the alkyl or alkylidene substituents of R<sup>1</sup> can be linked to form a 3 to 7-membered non-aromatic ring: and

wherein if X is nitrogen, X is linked to R<sup>1</sup> by a single bond and the terminal carbon of R<sup>1</sup> that links R<sup>1</sup> to N is saturated;

(4) R<sup>3</sup> (a) is hydrogen, (C1-C6) alkyl, or phenyl or phenylalkyl wherein the alkyl is C1 to C6 and either such phenyl can be substituted with the same substituents defined above for the aryl or heteroaryl of R<sup>xa</sup>, (b) is -R<sup>12</sup>Z(R<sup>xx</sup>)(R<sup>yy</sup>)(R<sup>11</sup>), wherein R<sup>12</sup> is bonded to N, Z is independently the same as X, R<sup>xx</sup> is independently the same as R<sup>x</sup>, R<sup>yy</sup> is independently the same as R<sup>y</sup>, R<sup>11</sup> is independently the same as R<sup>2</sup> and R<sup>12</sup> is independently the same as R<sup>1</sup>, or (c) forms, together with R<sup>4</sup>, a ring C, as follows:



, wherein R<sup>4\*</sup> is hydrogen when ring C is present;

(5) n is 0 or 1, and where if n is 1, R<sup>3\*</sup> is either (C1-C6) alkyl (with the attached nitrogen having a positive charge) or oxygen (forming an N-oxide) and X is carbon;

(5') Q together with the illustrated ring nitrogen and ring carbon bearing R<sup>5</sup> form ring C, wherein ring C is a 3 to 8-membered ring, a 3 to 8-membered ring substituted with a 3 to 6-membered spiro ring, or a 3 to 8-membered ring fused with a 5 to 6-membered ring, wherein the fused ring lacking the illustrated ring nitrogen can be aromatic or heteroaromatic, wherein for each

component ring of ring C there are up to two heteroatoms selected from oxygen, sulfur or nitrogen, including the illustrated nitrogen, and the rest carbon, with the proviso that the ring atoms include no quaternary nitrogens other than the illustrated nitrogen, with the proviso that, in saturated rings, ring nitrogen atoms are separated from other ring heteroatoms by at least two intervening carbon atoms:

wherein the carbon and nitrogen ring atoms of ring C can be substituted with substituents selected from (C1-C6) alkyl, (C2-C6) alkenylene, cyano, nitro, trifluoromethyl, (C2-C7) alkyloxycarbonyl, (C1-C6) alkylidene, hydroxyl, (C1 - C6) alkoxy, oxo, hydroxycarbonyl, aryl wherein the aryl is as defined for R<sup>xa</sup> or heteroaryl wherein the heteroaryl is as defined for R<sup>xa</sup>, with the proviso that ring atoms substituted with alkylidene, hydroxycarbonyl or oxo are carbon, with the further proviso that ring atoms substituted with hydroxyl or alkoxy are separated from other ring heteroatoms by at least two intervening carbon atoms;

- (6) R<sup>4</sup> and R<sup>4\*</sup> are independently hydrogen or (C1-C6) alkyl, or one of R<sup>4</sup> and R<sup>4\*</sup> can be (C1-C6) hydroxyalkyl; and
- (7) R<sup>5</sup> is (CO)NR<sup>13</sup>R<sup>14</sup>, (CO)OR<sup>15</sup>, (CO)SR<sup>16</sup>, (SO<sub>2</sub>)NR<sup>17</sup>R<sup>18</sup>, (PO)(OR<sup>19</sup>)(OR<sup>20</sup>), (CR<sup>22</sup>)(OR<sup>23</sup>)(OR<sup>24</sup>), CN or tetrazol-5-yl, wherein R<sup>13</sup>, R<sup>14</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup> and R<sup>20</sup> are independently hydrogen, (C1-C8) alkyl which can include a (C3-C8) cycloalkyl, wherein the carbon linked to the oxygen of R<sup>15</sup> or the sulfur of R<sup>16</sup> has no more than secondary branching and, (C2-C6) hydroxyalkyl, aminoalkyl where the alkyl is C2 to C6 and the amino can be substituted with up to two independent (C1-C6) alkyls, arylalkyl wherein the alkyl is C1-C6, heteroarylalkyl wherein the alkyl is C1 to C6, aryl or heteroaryl, R<sup>22</sup> is hydrogen or OR<sup>25</sup> and R<sup>23</sup>, R<sup>24</sup> and R<sup>25</sup> are (C1-C6) alkyl, phenyl, benzyl, acetyl or, where R<sup>22</sup> is hydrogen, the alkyls of R<sup>23</sup> and R<sup>24</sup> can be combined to include 1,3-dioxolane or 1,3-dioxane:

wherein the aryl is phenyl or naphthyl and the heteroaryl is a five-membered ring, a six-membered ring, a six-membered ring fused to a five-membered ring, a five-membered ring fused to a six-membered ring, or a six-membered ring fused to a six-membered ring, wherein the heteroaryl is aromatic and contains heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, with the remaining ring atoms being carbon;

wherein the aryl, heteroaryl, aryl or arylalkyl or the heteroaryl of heteroarylalkyl can be substituted with substituents selected from the group consisting of fluoro, chloro,

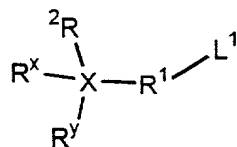
bromo, nitro, cyano, hydroxy, trifluoromethyl, amidosulfonyl which can have up to two independent (C1-C6) N-alkyl substitutions, (C1-C6) alkyl, (C2-C6) alkenyl, (C1-C6) alkylamine, dialkylamine wherein each alkyl is independently C1 to C6, amino, (C1-C6) alkoxy, (C2-C7) alkanoyl, (C2-C7) alkanoyloxy, trifluoromethoxy, hydroxycarbonyl, (C2-C7) alkyloxycarbonyl, aminocarbonyl that can be N-substituted with up to two independent (C1-C6) alkyl, (C1-C6) alkylsulfonyl, amidino that can substituted with up to three (C1-C6) alkyl, or methylenedioxy or ethylenedioxy with the two oxygens bonded to adjacent positions on the aryl or heteroaryl ring structure, which methylenedioxy or ethylenedioxy can be substituted with up to two independent (C1-C6) alkyl; and wherein R<sup>13</sup> and R<sup>14</sup> together with the nitrogen can form a 5 to 7-membered ring that can contain one additional heteroatom selected from oxygen and sulfur.

26. The method of claim 25, wherein the spasticity is associated with epilepsy, stroke, head trauma, multiple sclerosis, spinal cord injury or dystonia.

27. The method of claim 26, wherein the neurodegenerative disease is Alzheimer's disease, multi-infarct dementia, AIDS dementia, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis or stroke or head trauma.

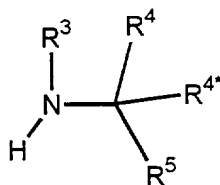
28. A method of synthesizing a compound of claim 1 comprising:

A) reacting a compound of one of the following formulas



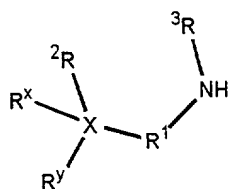
, wherein L<sup>1</sup> is a nucleophilic substitution leaving group, with a compound of the formula

2)



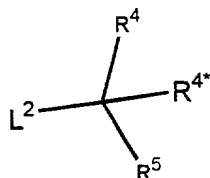
or B) reacting a compound of the formula

1)



, with a compound of the formula

2)



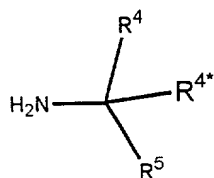
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, wherein  $\text{L}^2$  is a nucleophilic substitution leaving group.

29. A method of synthesizing a compound of claim 1 comprising:

A) reductively alkylating a compound of the formula

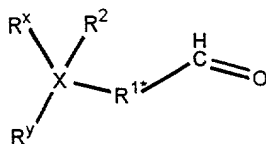
1)



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with a compound of the formula

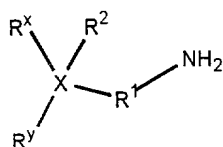
2)



, where  $\text{R}^{1*}$  differs from  $\text{R}^1$  in that it lacks the carbon that is part of the illustrated aldehyde carbonyl,

15 OR B) reductively alkylating a compound of the formula

1)

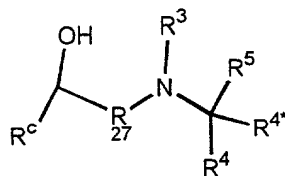


with a compound of the formula

2)

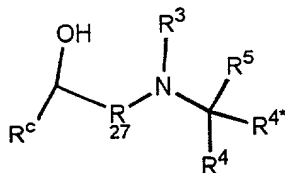






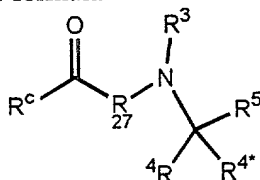
with another nucleophilic substitution leaving group.

33. The method of claim 32, comprising reacting a compound of formula

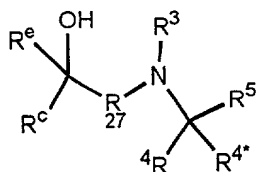


5 with a azodicarboxylate in the presence of a phosphine compound.

34. A method of synthesizing a compound of claim 1 comprising reacting  $R^eM$  with a compound of the formula



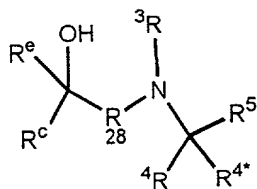
to form a compound of the formula



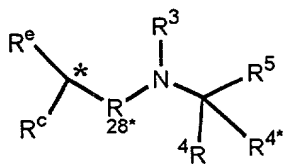
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, wherein  $R^e$  and  $R^c$  are independently the same as defined for  $R^x$ , wherein M is a metal-containing substituent such that  $R^eM$  is a organometallic reagent, and wherein  $R^{27}$  has the same definition as  $R^1$  except that it does not include a nitrogen, oxygen or sulfur and does not include any double bonds conjugated with the above-illustrated carbonyl.

15 35. A method of synthesizing a compound of claim 1 comprising dehydrating a compound of the formula

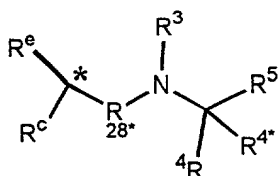


to form a compound of the formula

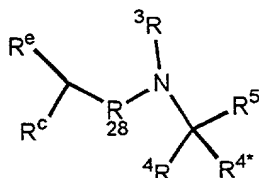


wherein C\* has a double bond with an adjacent carbon, and wherein R<sup>e</sup> and R<sup>c</sup> are independently the same as defined for R<sup>x</sup>, and wherein R<sup>28</sup> and R<sup>28\*</sup> have the same definition as R<sup>1</sup> except R<sup>28</sup> and R<sup>28\*</sup> do not include a nitrogen, oxygen or sulfur.

- 5                    36. A method of synthesizing a compound of claim 1 comprising reducing a compound of the formula



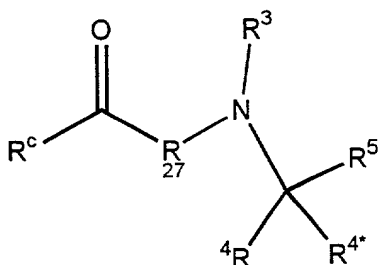
wherein C\* has a double bond with an adjacent carbon and R<sup>c</sup> is independently the same as defined for R<sup>x</sup>, to form a compound of the formula



10

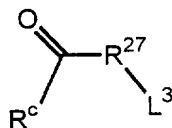
, wherein R<sup>e</sup> is independently the same as defined for R<sup>x</sup>, and wherein R<sup>28</sup> and R<sup>28\*</sup> have the same definition as R<sup>1</sup> except that R<sup>28</sup> and R<sup>28\*</sup> do not include a nitrogen, oxygen or sulfur.

37. A method of synthesizing a compound that can be used to synthesize the compound of claim 1, the method comprising synthesizing the compound of formula:

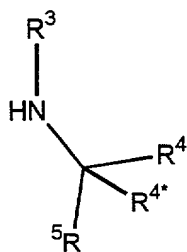


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wherein R<sup>c</sup> is independently the same as R<sup>x</sup>, said synthesis comprising reacting a compound of formula

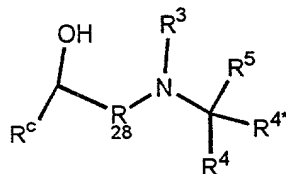


with a compound of formula

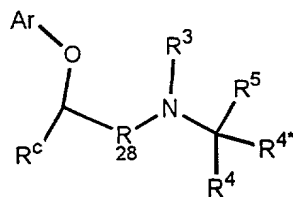


, wherein  $R^{27}$  has the same definition as  $R^1$  except that it does not include a nitrogen, oxygen or sulfur and does not include any double bonds conjugated with the above-illustrated carbonyl, and wherein  $L^3$  is a nucleophilic substitution leaving group.

38. A method of synthesizing of a compound of claim 1, the method comprising reacting a compound of formula

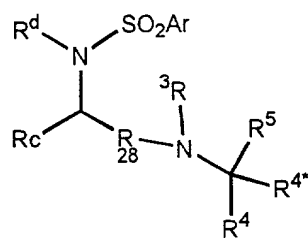


10 , wherein  $R^c$  is independently the same as  $R^x$ , with Ar-Q wherein Ar is aryl which is substituted with an electron-withdrawing group or heteroaryl which is substituted with an electron-withdrawing group, and wherein Q is fluoro or chloro to form



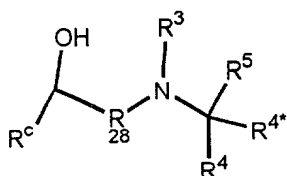
15 wherein  $R^{28}$  has the same definition as  $R^1$  except that  $R^{28}$  does not include a nitrogen, oxygen or sulfur.

39. A method of synthesizing a compound that can be used to synthesize the compound of claim 1, the method comprising synthesizing a compound of formula X:



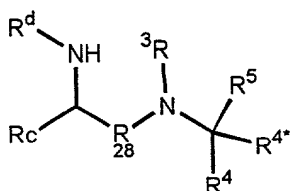
X

20 by reacting a compound of formula:

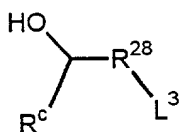


with  $R^d\text{NHSO}_2\text{Ar}$ , wherein  $R^c$  and  $R^d$  are independently the same as  $R^x$ , and Ar is aryl or heteroaryl, and wherein  $R^{28}$  has the same definition as  $R^1$  except that  $R^{28}$  does not include a nitrogen, oxygen or sulfur.

- 5                    40. The method of claim 39, further comprising converting the compound of formula X to:

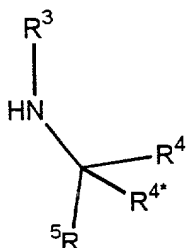


41. A method of synthesizing a compound that can be used to synthesize the compound of claim 1, the method comprising reacting a compound of formula

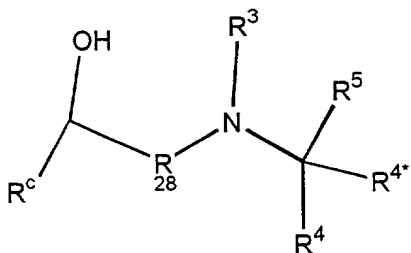


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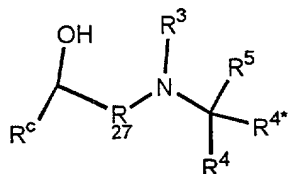
with a compound of formula



- , wherein  $L^4$  is a nucleophilic substitution leaving group, wherein  $R^c$  is independently the same as  $R^x$ , and wherein  $R^{28}$  has the same definition as  $R^1$  except that  $R^{28}$  does not include a nitrogen, oxygen or sulfur, to form a compound of formula
- 15



42. A method of synthesizing a compound that can be used to synthesize the compound of claim 1, the method comprising synthesizing the compound of formula:



wherein R<sup>c</sup> is independently the same as R<sup>x</sup> and R<sup>27</sup> has the same definition as R<sup>1</sup> except that

- 5 R<sup>27</sup> does not include a nitrogen, oxygen or sulfur and R<sup>27</sup> does not include any double bonds at the atom bonded to the above-illustrated hydroxyl-substituted carbon, said synthesis comprising reducing the ketone of a compound of formula

